

Elastic and viscous stiffness of the canine left ventricle

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TEMPLETON, GORDON H., AND LOUIS R. NARDIZZI. *Elastic and viscous stiffness of the canine left ventricle*. J. Appl. Physiol. 36(1): 123-127. 1974.—Elastic and viscous stiffness of canine left ventricles was measured continuously over the entire cardiac cycle. These mechanical properties were determined from the sinusoidally varying portion of the left ventricular pressure induced by an externally applied sinusoidal volume change with a constant peak amplitude of 0.5 ml and a frequency of 22 Hz. The sinusoidal pressure perturbations varied during the cardiac cycle both in peak amplitude and in the time of occurrence of the peak amplitude with respect to the volume changes that produced them. Determinations were made of ventricular stiffness, or elastance, which is defined as the ratio of the peak change in the pressure perturbations to the peak change in volume. Stiffness and the time difference between the occurrence of the peak volumetric perturbation and the corresponding peak of the pressure perturbation were used to calculate the elastic and viscous components of ventricular stiffness. These elastic and viscous components of stiffness increased proportionally with ventricular pressure, and the percentage change in elastic stiffness from diastole to systole was greater than that of viscous stiffness.

mechanical properties; elasticity; viscosity; inertia; stiffness; elastance; compliance; dog; model

PREVIOUSLY, THE TECHNIQUES used to measure the elastic and viscous stiffness of cardiac muscle have required that these parameters be measured separately, usually in strips of muscle, and during either contraction or rest. Diastolic elastic stiffness is measured by a variety of techniques which in general determine a ratio of a change in force to a dimensional change in either papillary muscle or an intact ventricle. On the other hand, elastic stiffness of active muscle is measured by the quick-release technique in papillary muscle, and diastolic viscous stiffness is measured by a quick-stretch method which evokes stress-relaxation.

A technique which measures elastic and viscous stiffness simultaneously has been developed by modifying an established technique for measuring ventricular stiffness (9-11). A sinusoidal volumetric forcing function is used to induce measurable sinusoidal perturbations in the left ventricular pressure wave form. From the peak value of each pressure perturbation (ΔP) and the peak value of the volume change (ΔV), a value of stiffness ($\Delta P/\Delta V$), or the equivalent term elastance, can be determined. By using a frequency of 22 Hz for the volume changes and pacing the heart at 2 Hz, 22 values of stiffness can be determined over one cardiac cycle. To measure elastic as well as viscous stiffness, a means for measuring the differences in time between the occurrence of the peak of each volume sinusoid and the peak of the corresponding pressure sinusoid was added to the technique for measuring stiffness. From these time measurements and the corresponding stiffness values, it was possible to determine a linear dynamic model for the intact

ventricle and to determine the elastic and viscous stiffness coefficients for the model.

METHODS

A detailed description of surgical procedures and instrumentation has been presented previously (9-11). Mongrel dogs were placed on complete heart-lung bypass. A balloon on the end of a fluid-filled cannula was inserted into the left ventricle through a stab incision in the apical dimple and filled with saline (Fig. 1). Both the inflow and outflow tracts of the ventricle were occluded with Teflon buttons. A piston on the external end of the cannula was driven sinusoidally to produce a peak volume change of 0.5 ml in the ventricle at a frequency of 22 Hz. Measurable sinusoidal pressure changes in the ventricle were produced by the volume changes as shown in Fig. 2, A-C. The heart was paced throughout the experiment in synchronization with the piston frequency. This pacing procedure allowed data to be averaged on a computer since the resulting out-of-phase pressure and volume perturbations began at the same values and with the same phase differences at the beginning of each ventricular pressure cycle.

The left ventricular pressure perturbations sensed by the pressure transducer (model P21, Konigsberg Instruments) were amplified by a carrier preamplifier and recorded on magnetic tape. Simultaneously, the volume perturbations produced by the flow-pulse generator were recorded by connecting a differential transformer (Sanborn 7DCDT-250) to the shaft of the piston and measuring the amplitude of the piston displacement. Full piston displacement was calibrated to produce 1 ml of volume change. The signal from the differential transformer was amplified with another carrier preamplifier and recorded on magnetic tape. The two carrier preamplifiers were appropriately connected together to eliminate phase shift introduced by the preamplifiers between the volume and pressure channels. The pacing stimulus which was in synchronization with a preset number of volume perturbations was recorded on a third channel of analog tape. The stimulus recording was used as a trigger signal to a PDP-12 computer for the purpose of digitizing the data at a sampling rate of 1,000/s and averaging the digitized volume and pressure perturbations for 16 ventricular pressure cycles. The digitized and averaged perturbed pressure and the volume and pressure perturbations are shown in Fig. 2, A, B, and C, respectively.

A Fourier series analysis of the wave forms in Fig. 2A was performed in order to subtract the unperturbed ventricular pressure wave form corresponding to the lower frequency terms in the Fourier spectrum. The resulting perturbed left ventricular pressure wave form shown in Fig. 2B was constructed using the 9th through the 45th harmonics of the wave form in Fig. 2A. These higher harmonics arose only from the forcing function. This lack of influence of ventricular contraction on these harmonics of ventricular pressure was concluded from our earlier study (11) which showed that a wave form constructed by the first 5 harmonics was identical to a pressure wave form containing 45 harmonics and generated in

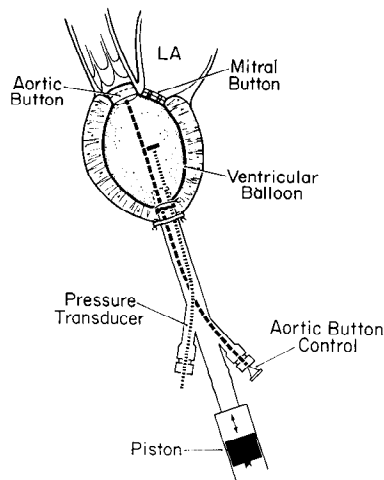


FIG. 1. Preparation of isovolumic ventricle in a dog showing the equipment used to induce small sinusoidal volume changes within the ventricle. The ventricle is made isovolumic by occluding inflow and outflow tracts of the ventricle with Teflon buttons, inserting a balloon through a stab incision in the apical dimple, and filling it with saline. Sinusoidal movement of the piston induces in the ventricle a sinusoidal volume change with a peak amplitude of 0.5 ml at a frequency of 22 Hz. Pressure transducer is used to measure left ventricular pressure which includes a measurable sinusoidal response to the induced volume changes.

the same heart without the sinusoidal volume changes being induced. The time difference between the occurrence of a peak of the volume perturbation and the corresponding pressure perturbation was calculated and is shown in Fig. 2, *B* and *C*. This time difference or phase angle was used to calculate the dynamical components of left ventricular stiffness throughout an average cardiac cycle. The system used to generate the sinusoidal volume perturbations was calibrated to determine the inherent time delay within the system between the piston movement and the pressure response. This was done with the balloon outside of the heart. With the balloon in place on the end of the fluid-filled cannula, saline was introduced so that different volumes simulated progressively increasing operating pressures from 20 to 120 mmHg. With the pressure within the system initially held constant at 20 mmHg, the time delay was determined between the peak of the volume perturbation, measured by a differential transformer attached to the piston, and the peak of the pressure perturbation, measured by the pressure transducer within the balloon. This measurement was then repeated as the pressure within the balloon was increased in 10-mmHg increments to a maximal pressure of 120 mmHg. No phase displacement between the volume and pressure perturbations was measured while the mean system pressure was below 90 mmHg. Above this pressure, a maximum phase angle of 6° was determined. This error is small but does account for some inaccuracies at the peak of systole.

Another source of error which may be introduced by this technique is the slippage which could occur between the balloon and endocardium during the rapid sinusoidal volume changes. If present, this slippage would influence the resistance to stretch and the size and shape of the pressure perturbations. This slippage cannot be measured, and consequently the error due to slippage in the stiffness measurements is unknown.

THEORETICAL CONSIDERATIONS

The simultaneous recording of the sinusoidal pressure and volume from the left ventricle indicated that the volume changes were lagging behind the pressure changes. That is, a phase displacement exists between the change in volume and the pressure developed

by the left ventricular muscle. In addition, the small sinusoidal volume perturbations of constant amplitude induced small sinusoidal pressure perturbations which increased in amplitude from diastole to systole. These results make possible the analysis of the mechanics of the intact left ventricle by a linear dynamical model.

Choosing a linear versus a nonlinear model for the dynamic response of the left ventricle is an approximation. The choice of a linear system is based on the sinusoidal response in pressure of the ventricle to the sinusoidal volumetric forcing function. A more rigorous proof of system linearity would require tests for additivity and homogeneity, since these properties mathematically define a linear system (3, 5, 12). Additivity, or superposition, is proven by adding two simultaneous volume changes and observing whether the pressure response is the sum of the individual responses to each input. Homogeneity is satisfied if the amplitude changes of volume proportionally alter the output amplitudes of pressure at the given input frequency (3).

These direct tests for additivity and homogeneity cannot be applied to the ventricle since the amplitude of the sinusoidal volume change cannot be altered in any given ventricle, and since multiple volume changes cannot be applied simultaneously to the ventricle using the available equipment. However, one aspect of linear systems was shown by transforming to the frequency domain the sinusoidal volume and pressure wave forms obtained during ventricular diastole and fibrillation. These two ventricular states were chosen since developed pressure was constant. The frequency re-

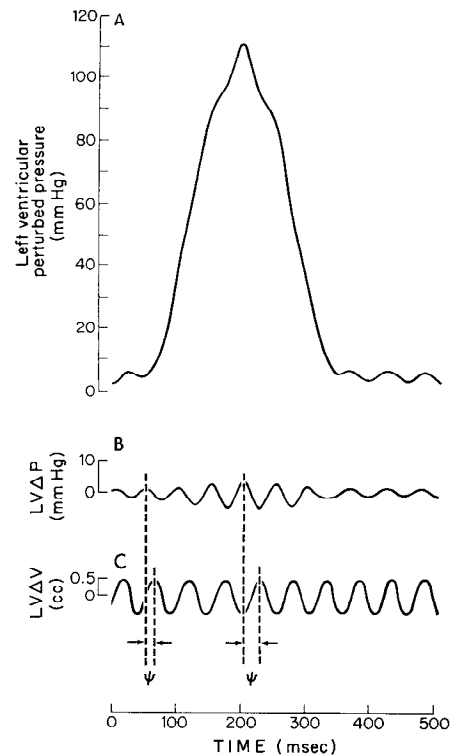


FIG. 2. Variations of pressure and volume in an isovolumic ventricle during a cardiac cycle showing the influence of a sinusoidal forcing function. Sinusoidal variation in ventricular volume, shown at the bottom of the figure (*C*), induces sinusoidal perturbations in the ventricular pressure, shown at the top (*A*). Fourier analysis is used to extract the variations in ventricular pressure resulting from the sinusoidal volume changes. Middle wave form (*B*) shows the sinusoidal pressure response of the ventricle. See text for an explanation of the variation in both the amplitude of the pressure perturbations and the displacement in time, Ψ , between peak in volume wave form and corresponding peak of pressure wave form. With respect to Ψ , note that pressure leads the volume and that the magnitude of Ψ varies during the cardiac cycle.

sponse of the volume wave form showed a large modulus at the fundamental frequency of 22 Hz with small moduli at the harmonics on either side. The moduli for frequencies away from the perturbation frequency were zero. These harmonics arose due to the nature of the cam used to generate the volume changes and possibly to the modification of the frequency distribution of the volume wave form by the sampling frequency. The same frequencies were contained in both the pressure and volume frequency distributions, and this observation is an aspect that characterizes a linear system with constant parameters (3).

As seen in Fig. 2B, the peak magnitude of the pressure perturbations and the phase displacement, Ψ , are constant during diastole when the average ventricular pressure is constant, but both parameters increase with pressure during systole. This dependence of both the magnitude and phase of the pressure perturbations on developed pressure indicates that elastic and viscous stiffness also vary with pressure. However, the linear second-order differential equation used as the model can be considered to have constant coefficients if the developed pressure and active state are changing relatively slowly with respect to the period of a volume perturbation. Then each pressure perturbation can be analyzed as if it were a pure sine wave at that particular developed pressure and active state, both during diastole and systole.

The pressure perturbation produced by the sinusoidally alternating volume, $V_0 \cos \omega t$, of amplitude V_0 and angular frequency ω is given by

$$P(t) = P_0 \cos(\omega t + \Psi) \quad (1)$$

where P_0 is the amplitude of the pressure change and Ψ is the phase difference expressed in degrees between the pressure and the volume sinusoids as shown in Fig. 2, B and C. If Ψ is a positive angle, then the pressure perturbation is leading the volume perturbation or the volume perturbation is lagging behind the pressure perturbation. Hence, the mechanics of the muscle can as a first approximation be described by a linear time-varying model such as

$$\frac{1}{K} \frac{d^2 P(t)}{dt^2} + \frac{1}{\eta} \frac{dP(t)}{dt} + \frac{1}{m} P(t) = \frac{1}{\alpha} \frac{d^2 V(t)}{dt^2} \quad (2)$$

where K is the elastic stiffness, η is the viscous damping, m is the equivalent mass, and α is a constant relating linear displacement to spherical volume changes. Assuming an ideal spherical ventricular cavity of 33.3 cm³ having an effective area of 50 cm², α can be computed to be 77 cm⁴ for the equipment used.

Equation 2 is a simple three-element model whose output is pressure and input is volume displacement. The linear model consists of elastic, viscous, and inertial elements which are represented, respectively, by the components of the sum in Eq. 2. The mathematical expressions composing the sum were derived from the definitions of the parameters for linear systems (3). For a linear system in which pressure and volume are parameters, the pressures of elastic, viscous, and inertial elements are proportional to volume and its first and second derivatives with time, respectively. This model does not explicitly take into account the thickness, geometry, compressibility, and anisotropic properties of the ventricular wall.

Inserting Eq. 1 into 2 yields the expressions for viscous stiffness and elastic stiffness at any particular ventricular pressure.

viscous stiffness

$$\eta\omega = \frac{\alpha P_0}{V_0 \sin \Psi} \quad (3)$$

elastic stiffness

$$K = \frac{\alpha m \omega^2 P_0}{V_0 m \omega^2 \cos \Psi + P_0 \alpha} \quad (4)$$

Note that if $V_0 m \omega^2 \cos \Psi \gg P_0 \alpha$ or equivalently if $K \ll m \omega^2$, then the elastic stiffness can be simplified to

$$K = \frac{\alpha P_0}{V_0 \cos \Psi} \quad (5)$$

This simplified equation for K is not applicable for the present study when ventricular mass was greater than 50 g, but could apply possibly in studies of muscle strips. The stiffness ratio SR is defined as the ratio of viscous to elastic stiffness

$$SR = \frac{\eta\omega}{K} \quad (6)$$

The total stiffness at any particular time in the cardiac cycle is simply

total stiffness

$$= \frac{1}{\sqrt{(1/K)^2 + (1/\eta\omega)^2}} = \frac{\alpha P_0}{V_0} \quad (7)$$

where P_0 and V_0 are the amplitudes of the perturbations and α is a constant equal to 77 cm⁴.

Finally, Young's modulus which is a ratio of stress to strain in the ventricular wall can be expressed as

$$E = \frac{\alpha P_0}{V_0/V} \quad (8)$$

where V is the average volume of the ventricular cavity. For the calculations made in this study, a value for V of 33.3 cm³ was used.

RESULTS

As shown in Fig. 2, A and B, the peak values of the pressure perturbations are directly related to ventricular pressure. To determine whether this increase in amplitude of the perturbations with higher pressure was a result of an increase in elastic stiffness, a decrease in viscous damping, or a combination of both, elastic and viscous stiffness was calculated and plotted with respect to ventricular pressure. Viscous stiffness, the reciprocal of viscous damping, and elastic stiffness were calculated using Eq. 3 and 4 from the peak values of both the pressure perturbations (P_0) and the volume perturbations (V_0) and from the phase angles (Ψ) associated with each pair of pressure and volume perturbations. Figs. 3 and 4 show the variations of viscous and elastic stiffness with pressure for four dogs. These results indicate that the elastic and viscous stiffness is of the same order of magnitude and that the increased total stiffness at higher pressures results from increases in both the elastic and viscous components of stiffness. Moreover, further comparison of the curves in Fig. 3 with those of Fig. 4 shows that, from diastole to systole, the elastic component of stiffness increases by an order of magnitude while the viscous component increases by less than a factor of four. Consequently, the increase in total stiffness with ventricular pressure during a cardiac cycle is primarily due to an increase in the elastic component of stiffness.

Figure 5 shows the relationship between ventricular pressure and the stiffness ratio, which is simply the ratio between viscous and elastic stiffness. The stiffness ratio initially declines with the increase in pressure due to ventricular contraction but rises slightly near the peak of systole as pressure continues to rise. The overall decline in the stiffness ratio from diastole to systole reflects the observation mentioned before that the variation in total stiffness with pressure depends primarily on the elastic component of stiffness rather than on its viscous component. The reason for the reversal of the indirect relationship between the stiffness ratio and pressure at the peak of systole is unknown.

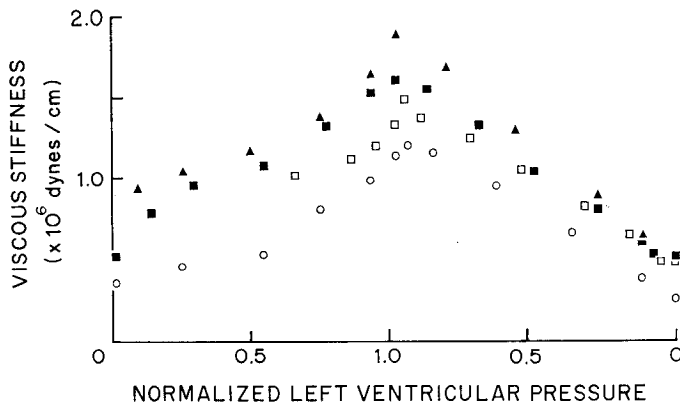


FIG. 3. Relationship between viscous stiffness and ventricular pressure during the cardiac cycle. Each symbol represents a different dog and each point is an average value obtained from 16 cardiac cycles.

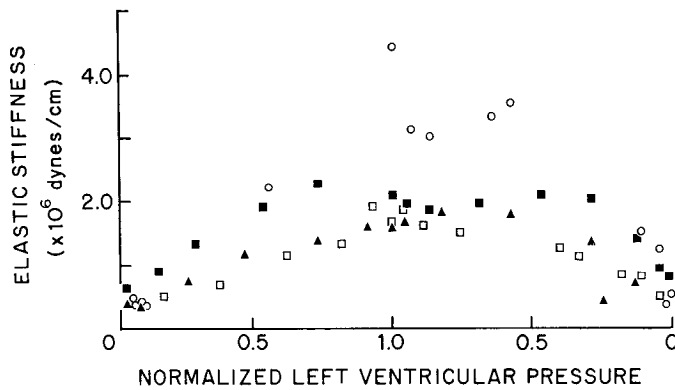


FIG. 4. Variation between elastic stiffness and ventricular pressure during the cardiac cycle. Each symbol represents a different dog and each point is an average value obtained from 16 cardiac cycles.

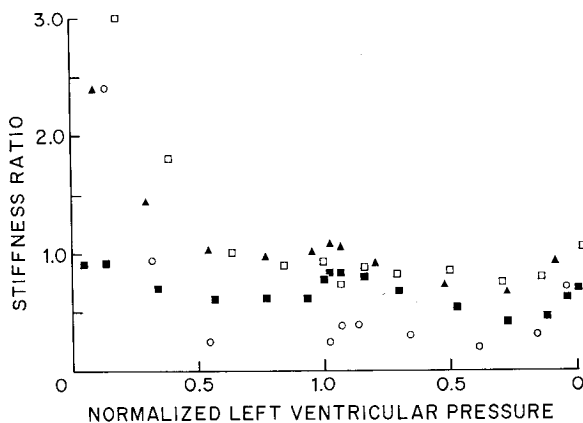


FIG. 5. Relationship between ventricular pressure and stiffness ratio, defined as the ratio between viscous and elastic components of stiffness.

DISCUSSION

Many techniques have been developed for measuring the elastic and viscous stiffness of cardiac muscle. The reason for this development is that the measurement of the elastic and viscous nature of the heart has proven useful in describing muscular contraction, in understanding the mechanism of contraction, and in describing the influence of various interventions on muscular contraction. The technique used for measuring viscous stiffness involves quickly

stretching the muscle and observing either stress-relaxation, a transient change in tension induced by an instantaneous change in length, or creep, a transient change in length induced by an instantaneous change in tension. The elastic stiffness of resting muscle is determined from the slope of length-tension diagrams and from measurements of diastolic compliance ($\Delta L/\Delta T$), where ΔT is the change in muscle tension induced by a change in muscle length, ΔL . Elastic stiffness of contracting muscle involves evoking a quick release (ΔL) and measuring the change in tension (ΔT) (8).

The elastic stiffness or elastic modulus is defined as the ratio of a change in stress or force to a change in strain or per unit change in length and should not be confused with elasticity. Elastic stiffness is dependent only upon the change in length and independent of the time required to change the length. Consequently, the elastic stiffness is referred to as a static property and usually not as a dynamic or time-dependent property. In view of this definition, a technique used to measure elastic stiffness should determine the change in tension resulting only from the induced change in length and not that resulting from how rapidly the length change occurred. This criterion for measuring elastic stiffness can be satisfied when using a length-tension diagram if after a change to a new muscle length, sufficient time is allowed for stress-relaxation to disappear before tension is measured. Consequently, this approach can be used only for noncontracting muscle. This criterion for measuring elastic stiffness can be satisfied also with techniques which induce quick changes in length or volume and measure the simultaneous instantaneous change in tension if the stretch is very rapid. Theoretically, this technique requires a stretch with zero velocity (or infinite time rate of change in tension) to eliminate any influence on tension by viscosity. Accordingly, a possible criticism of this technique is that the elastic stiffness measurement made by it probably includes a viscous component since a finite time is required for the stretch.

The determination of viscous stiffness by means of a quick stretch or release requires a finite time before the change in tension or length can be measured. Consequently, this technique can be used only during long diastolic intervals when the only change in tension is caused by the externally applied stretch.

The use of a sinusoidal forcing technique to measure elastic and viscous stiffness offers some advantages over the cited classical techniques. The application of sinusoidal stretches to muscle is similar to the quick-stretch techniques with respect to the rapidity of the stretches, but unlike the technique used to measure the series elastic element stiffness the sinusoidal technique does not ignore the response of the viscous property to the stretch. In addition, unlike the cited techniques, the use of a sinusoidal forcing function allows measurement of the elastic and viscous stiffness over the entire cardiac cycle during both diastole and systole.

Sinusoidal forcing functions have been used previously to measure both components of stiffness in strips of muscle. After Gasser and Hill (4) proposed its use, Buchthal and his coworkers (1), in skeletal muscle, and Lundin (6), using strips of ventricular muscle from frogs, measured elastic and viscous stiffness. Recent studies using this technique (2, 7) have utilized linear second-order models to divide stiffness into its elastic and viscous components. These models are similar to the one used in the present study with the major exception being the neglect of the inertial contribution by Machin and Pringle (7). This assumption that inertia is negligible was made by this study since small strips of muscle with small mass were involved and since the phase angles, being sufficiently small, indicated that the inertial component was negligible with respect to the elastic component. This assumption that mass is negligible is not always possible using the technique involving whole ventricles, however. Several dogs have displayed phase angles greater than 90° which implies that the coefficient for inertia is not negligible with respect to the other coefficients in the model.

The dependence of the elastic and viscous stiffness on ventricular pressure shown by the present study concurs with the results of other studies with strips of other types of muscle. For instance, Buchthal and Rosenfalck (2) by modeling the response of a skeletal muscle strip with a linear second-order system showed that elastic and viscous stiffness was directly related to developed tension.

As shown in Figs. 3, 4, and 5, the relationship between ventricular pressure and either viscous or elastic stiffness varies from dog to dog. All of the reasons for this variation are unknown. Part of the variation possibly results from differences in ventricular size and wall thickness. The influence of these variables could possibly

be eliminated by using some model to translate the stiffness-pressure relationships now used to stiffness-tension relationships where the new stiffness parameter would be a ratio of tension and length. Other factors which could possibly influence the variation from dog to dog could be differences in the geometrical arrangement of muscle fibers or a variable content of muscle and connective tissue within the hearts. Further, it remains to be seen how viscous and elastic stiffness is related to the contractile state of the myocardium. If such a relationship exists, then a variation of these components of stiffness from dog to dog would be expected.

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